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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KWON, BRIAN YONG S	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 08/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,257	BUCHANAN ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-23 and 26* is/are pending in the application.

4a) Of the above claim(s) *11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10, 12, 14-23 and 26* is/are rejected.

7)☒ Claim(s) *13 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Withdrawal of Allowability

1. The examiner has indicated in O.A. (Qualye Action) mailed February 12, 2004 that claims 10-23 are in condition for allowance except formality of the claims, namely canceling of non-elected claims. In reconsideration and in light of newly amended claim (claim 11), the examiner withdraws the allowability of claims 10-23.

Status of Application

2. By an amendment filed April 12, 2004, claims 1-9, 24-25 and 27-32 have been cancelled and claim 11 has been amended. Claims 10-23 and 26 are currently pending.

3. With respect to the claim 11, it appears that applicant's amending of claim 11 resulted from inadvertent inclusion of claim 11 in the allowed claims. The subject matter of the claim 11 has been restricted, and withdrawn from further consideration as a non-elected invention (See page 2 of O.A. mailed on August 26, 2002).

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

5. Applicant's reference to "ethyl-eicosapentaenoic, oleic, linoleic, alpha-linolenic, stearidonic, gamma-linolenic, dihomogammalinolenic, arachidonic, docosapentaenoic

and docosahexaenoic" in claim 20 is not complete without ending "acid", and should be corrected as "ethyl-eicosapentaenoic acid (ethyl-EPA), oleic acid, linoleic acid, alpha-linolenic acid, stearidonic acid, gamma-linolenic acid, dihomogammalinolenic acid, arachidonic acid, docosapentaenoic acid and docosahexaenoic acid (DHA)".

6. Claims 12-13 and 14 are objected. The abbreviation of EPA, DHA, ethyl-EPA or ethyl-DHA may not necessarily refer to applicant's intended eicosapentaenoic acid, docosahexaenoic acid, ethyl- eicosapentaenoic acid or ethyl- docosahexaenoic acid. For instance, DHA may refer to totally different compound such as dihydroxyacetone. Similarly, EPA may refer to 2-phenylbutyryl urea or ethylphenacemide. Applicant is requested to spell out the abbreviated terms such as EPA and DHA.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 15, 17-20 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present claim is drawn to a composition comprising 13-hdyroxyoctadeca-9Z, 11E-dienoic acid (13-HODE) in its free form and omga-3 fatty acid selected from EPA, DHA, a derivative of EPA and a derivative of DHA, and optionally carrier.

The instant specification discloses a composition comprising 13-HODE either in its free from or with a pharmaceutically acceptable carrier, auxiliary or excipient, wherein the carrier, auxiliary or excipient may be mono-, di- or triglyceride oil, corn, sunflower, safflower, cottonseed, grape seed, olive, evening primrose, borage, fish body and fish liver oils, or an ester of a fatty acid containing 16-26 carbon atoms and one or more double bonds; wherein the ester may be ethyl-eicosapentaenoic (ethyl-EPA), oleic, linoleic, alpha-linoleic, stearidonic, gamma-linolenic, dihomogammalinolenic, arachidonic, docosapentaenoic or docosahexaenoic (DHA) (page 16, lines 4-12). The specification also discloses that said composition may include emulsifying agents, antioxidants (e.g., ascorbyl palmitate, tocopherols and ascorbic acid), buffering agents, preservatives, humectantas, penetration enhancers, chelating agents, gelforming agents, ointment bases, perfumes and skin protective agents (page 21, lines 2-136). The specification is based on applicant's alleged discovery of finding of "stable" composition by incorporating 13-HODE into a triglyceride oil carrier or an ester of a fatty acid containing 16-26 carbon atoms and one or more double bonds (page 25, lines 3-4; page 26, lines 20-23), particularly EPA and DHA, more particularly ethyl ester of EPA (page 25, lines 10-14; page 26, line 23 thru page 27, line 2).

As preferred embodiment of the invention, the pharmaceutical composition of 13-HODE in combination with carrier selected from the group consisting of corn, sunflower, safflower, cottonseed, grape seed, olive, evening primrose, borage, fish body, fish liver oils, ethyl-eicosapentaenoic (ethyl-EPA), oleic, linoleic, alpha-linoleic, stearidonic, gamma-linolenic, dihomogammalinolenic, arachidonic, docosapentaenoic and docosahexaenoic (DHA), specifically a combination product containing 13-HODE in

combination with corn oil or an ethyl ester of a 16-26 carbon fatty acid with one or more double bonds, such as ethyl-oleate, ethyl-linolate, ethyl-EPA or ethyl-DHA (page 22, lines 1-18). As another preferred embodiment of the invention, the pharmaceutical combination containing 13-HODE and omega-3 fatty acids, like EPA, DHA, derivatives of EPA and DHA, ethyl-EPA and ethyl-DHA is disclosed (page 22, lines 22-24).

As discussed above, the specification provides sufficient written description for the composition comprising (A) 13-HODE and (B) omega-3 fatty acids selected from the group consisting of EPA, DHA, ethyl-EPA and ethyl-DHA, or the composition comprising (A) 13-HODE and (C) carrier selected from the group consisting of a mono-, di- or triglyceride oil; corn, sunflower, safflower, cottonseed, grape seed, olive, evening primrose, borage, fish body, fish liver oils; an ester of a fatty acid containing 16-26 carbon atoms and one or more double bonds (e.g., oleic, linoleic, alpha-linoleic, stearidonic, gamma-linolenic, dihomogammalinolenic, arachidonic and docosapentaenoic). The specification clearly does not provide an adequate representation regarding the composition comprising (A) 13-HODE, (B) omega-3 fatty acid selected from the group consisting of EPA, DHA, a derivative of EPA and a derivative of DHA and (C) carrier selected from the group consisting of a mono-, di- or triglyceride oil; corn, sunflower, safflower, cottonseed, grape seed, olive, evening primrose, borage, fish body, fish liver oils; and an ester of a fatty acid containing 16-26 carbon atoms and one or more double bonds (e.g., oleic, linoleic, alpha-linoleic, stearidonic, gamma-linolenic, dihomogammalinolenic, arachidonic and docosapentaenoic, made by the presently claimed invention. In other words, the specification provides insufficient written description to support the instantly required (A)/(B)/(C) combination. None of the

claimed compositions in claims 15-20 meets the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of the above mentioned (A) and (B) combination or (A) and (C) combination, the skilled artisan cannot envision (A)/ (B)/(C) or (B)/(C) combination.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

8. Claims 12 and 14-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for term "ethyl-EPA and ethyl-DHA", does not reasonably provide enablement for term "a derivative of EPA and a derivative of DHA". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention in summarized in In re Wands, 8 USPQ 1400 (CAFC 1988) at 1404 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls) at 547 the court recited eight factors: 1) the quality of experimentation necessary, 2) the amount of direction or guidance provided, 3) the presence of absence of working example, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability of the art, and 8) the breadth of the claims.

Although the specification describes that any derivatives of EPA or DHA would be useful for the claimed invention, the specification fails to provide sufficient working examples. In the instant case, Ethyl-EPA and ethyl-DHA are set forth as only examples of "a derivative of EPA or DHA". The specification does not provide sufficient directional guidance in how to make the claimed "a derivative of EPA or DHA", and fails to teach whether all compounds (derivatives of EPA or DHA) that are potentially suitable

for the invention would work similarly as to Ethyl-EPA and ethyl-DHA, without undue amount of experimentation.

It is generally known that each specific lipid has its own specific properties which depend on its precise chemical composition and which not necessarily possessed by other specific lipids. Therefore, the skill artisan would have not known in absence of sufficient directional guidance that which compounds of the claimed EPA or DHA derivatives are capable of accomplishing the desired result of the claimed invention without undue amount of experimentation.

The instant inventions are drawn to a pharmaceutical composition comprising 13-HODE and an omega-3-fatty acid such as EPA, DHA or a derivative of EPA or DHA (claims 14-23) and a method of reducing the inhibition of endogenous 13-HODE synthesis with administration of said composition (claim 12). The specification discloses that the incorporation of 13-HODE into triglyceride oil carrier or an ester, particularly ethyl ester of EPA, provides "stable" composition without degradation with many desirable effects including "inhibiting endogenous 13-HODE synthesis" (page 25, lines 2-3 and 10-11; page 26, line 20 thru page 27, line 2).

Given the broadest reasonable interpretation, the breadth of the instant claims encompasses glycerides of EPA or DHA, phospholipids of EPA or DHA, choline compounds of EPA or DHA, di or triglycerides of EPA or DHA, nicotinic acid compounds of EPA or DHA, amino acid compounds of EPA or DHA, esters of EPA or DHA or amides of EPA or DHA, C_{20}-n, ω-3 fatty acids.

As discussed above, although the specification describes working examples of ethyl-EPA and ethyl-DHA as derivatives of EPA and derivatives of DHA and the utility

of ethyl-EPA in providing "stable" composition and "inhibiting endogenous 13-HODE synthesis", there is no teaching in the specification that all derivatives of EPA and DHA (e.g., glycerides, phospholipids, choline compounds, di or triglycerides, nicotinic acid compounds and amino acid compounds of EPA or DHA and C_{20}-n, ω-3 fatty acids) would have similar properties as ethyl-EPA and ethyl-DHA. In view of limited numbers of working examples, the insufficient amount of guidance present in the specification, the nature of the invention, the state of art, the relative skills of the artisan and the predictability of the pharmaceutical art where many specific differences or different physicochemical properties are existed between each specific fatty acids or lipids, numerous possible derivatives of EPA and derivatives of DHA that may fall within the scope of the instant claims would take "undue painstaking experimentation" to determine said derivatives, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention.

9. Claim 10 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's recitation of "which may occur" renders the subject matter of said claim 10 unclear. Applicant's recitation of such term allows for the claim interpretation that the claimed underlying mechanism doesn't have to occur at all, and leaves the reader in doubt as to the meaning of the invention to which they refer.

Claim 20 recites that docosahexaenoic is "ethyl-DHA". Docosahexaenoic acid is generally recognized in the art as "DHA", not "ethyl-DHA". Apparently, this

inconsistency leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 14-23 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vanderhoek (US 60777525) in view of Breivik et al. (US 5502077).

Vanderhoek teaches the use of conjugated linoleic acids (CLAs) such as 13-HODE for inhibiting platelet aggregation (column 1, lines 3-7; column 2, lines 20-28; column 3, lines 25-36 and 55) or reducing LDL-cholesterol level (column 1, lines 42-49).

Breivik teaches the use of fatty acid composition comprising omega-3-fatty acids such as EPA, DHA and ethyl ester form of EPA or DHA, antioxidants (e.g., ascorbic acid, d-alpha tocopherol) and additives (e.g., colouring agents) for inhibiting platelet aggregation (Table 10; column 9, lines 65-66) or lowering LDL-cholesterol level (Table 8; column 9, lines 25-28; column 11, lines 14-38).

With respect to claims 14-17, 19-21, 23 and 26,

The teaching of Vanderhoek differs from the claimed invention in (i) the combination of 13-HODE, and omega-3 fatty acid (i.e., EPA, DHA, ethyl-EPA and ethyl-DHA); (ii) the inclusion of the specific carrier (e.g., mono, di- or triglyceride oil, specifically corn, sunflower, safflower, conttonseed, grape seed, olive, evening primrose, borage, fish body or fish liver oils, an ester of a fatty acid containing 16-26 carbon atoms

and one or more double bonds, , more specifically ethyl-EPA, oleic, linoleic, alpha-linoleic, stearidonic, gamma-linlenic, dihomogammalinolenic, arachidonic, docosapentaenoic and docosahexenoic acid); (iii) the specific dosage amount of 13-HODE; (iv) the specific dosage form; and optionally (v) further comprising antioxidants (e.g., ascorbic acid, d-alpha tocopherol) and additives (e.g., colouring agents). To incorporate such teaching into the teaching of Vanderhoek, would have been obvious in view of Breivik teaches the use of fatty acid composition comprising omega-3-fatty acids such as EPA, DHA and ethyl ester form of EPA or DHA, antioxidants (e.g., ascorbic acid, d-alpha tocopherol) and additives (e.g., coloring agents) for inhibiting platelet aggregation or lowering LDL-cholesterol level.

The above references in combination make clear that the use of 13-HODE, omega-3 fatty acids such as EPA, DHA, ethyl-EPA and ethyl-DHA and antioxidants for inhibiting platelet aggregation or lowering LDL-cholesterol level are well known in the art. It is obvious to combine two or three compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component.

With respect to claims 15, 17-20, when said carrier is ethyl-eicosapentaenoic acid (EPA) or docosahexaenoic acid, the scope of the claimed composition in claims 15, 17 and 19-20 overlaps to the scope of claim 14 composition. Therefore, the reference in combination makes obvious the claimed composition.

With respect to the specific dosage of 13-HODE (claim 16) and the specific dosage forms (claim 21), those of ordinary skill in the art would have readily optimized

effective dosages amounts or dosage forms as determined by good medical practice and the clinical condition of the individual patient. Determination of appropriate dosage amounts of each ingredients in said composition or dosage forms involving each of the above mentioned formulations would have been apparent to those of ordinary skill in the art, and routinely made by those of ordinary skill in the art and be within the ability of tasks routinely performed by them without undue experimentation.

Although the instant claims use the different names for the said ingredients than those taught in the cited references, these references are particularly pertinent and relevant because all the claimed species and their roles are well taught in the cited reference. Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Allowable Subject Matter

11. Claims 13 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Conclusion

12. No Claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

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